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Re: Does the Visibility of Grade Group 1 Prostate Cancer on Baseline Multiparametric

Magnetic Resonance Imaging Impact Clinical Outcomes?

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Letter to the editor

Re: Does the Visibility of Grade Group 1 Prostate Cancer on Baseline Multiparametric Magnetic Resonance Imaging Impact Clinical Outcomes? Deniffel D, Salinas E, Ientilucci M, Evans AJ, Fleshner N, Ghai S, Hamilton R, Roberts A, Toi A, van der Kwast T, Zlotta A, Finelli A, Haider MA, Perlis N. DOI: 10.1097/JU.0000000000001157

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We would like to congratulate Deniffel and colleagues for their excellent study, which provides further evidence that the clinical trajectory of actively surveyed, magnetic resonance imaging (MRI)-visible prostate cancer is distinct from that of non-visible disease. We could not help but noting that the first key finding of the study, i.e. that the hazard of treatment almost doubles in men with equivocal (HR 2.02; 95%CI: 1.11-3.68) or positive (HR 1.93; 95%CI: 1.21-3.09) baseline MRI, is remarkably similar to results from the University College London Hospital active surveillance (AS) cohort (Stavrinides et al., 2020):[1] in separate analyses not included in our original report, the HR for treatment in men with Likert 4-5 disease was 1.93 (95% CI: 1.44-2.59) after adjusting for Gleason grade, whereas other baseline predictors such as age or prostate specific antigen were either far less important or insignificant. Interestingly, although deeming Prostate Imaging-Reporting And Data System/Likert 4-5 as visible disease is appropriate for the detection of high-grade cancer, Deniffel and colleagues report that treatment-free survival is associated with baseline MRI even when this is indeterminate.

This dependence on baseline MRI visibility persisted in the absence of upgrading on follow up biopsies, despite that the hazard of upgrading was double in men with a positive baseline MRI compared to those with a negative one (HR 2.03, 95%CI: 1.06-3.86). This implies that once a cancer has been designated as MRI-visible, its clinical fate in an imaging-based AS pathway is likely to be early treatment, without upgrading events necessarily driving this tendency. This is reminiscent of the study by Eineluoto and colleagues, where progression on serial MRI was associated with protocol-based treatment change but not necessarily with upgrading, despite that baseline MRI was associated with both (Eineluoto et al., 2017).[2]

Whatever the clinical course during AS, the hazard of upgrading on radical prostatectomy (RP) in the Toronto report quadrupled in those with a positive baseline MRI (HR 4.45, 95% CI: 1.19-18.37). Many authors have previously reported that MRI-conspicuous Gleason Grade Group 1 (i.e. Gleason score = 6) cancers are associated with adverse features at surgery in surveillance candidates (Zhai et al., 2018),[3] but observing the same association at AS exit is a very exciting finding.

However, we should not be hasty to infer that the natural evolution of MRI lesions is the main driving force behind these results. In imaging-based AS cohorts without prescriptive monitoring protocols, ascertainment bias arising from the tendency to closely monitor visible lesions could be a factor at play. This practice is justified because the more conspicuous lesions appear to progress more over time (Ghavimi et al., 2018; Giganti et al., 2018),[4,5] but we should not treat the clinical trajectory of MRI-surveyed prostate cancer and its natural history as identical. However, MRI-based pathways, on the whole, seem to improve AS candidate selection (Klotz et al., 2020),[6] making it more likely that biopsy upgrades or adverse RP pathology at the end of AS reflect true oncological progression. We undoubtedly have made huge strides in the last decade, but new, well-designed studies and sophisticated methodologies for analysing longitudinal data are necessary to begin addressing these exciting questions.

Disclosures:

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